

Memorandum: N. E. Morton

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Outline of a program in medical genetics, with special reference to the first year, 1956-57

The proposed program in medical genetics has four functions: teaching and consultation; research in physiological and microbial genetics; collaboration in clinical, physiological, and statistical programs in the medical school; and research in the statistical methodology of human genetics. The emphasis placed on each of these depends on the opportunities and requirements of the medical school and the limitations of the genetics faculty, but a successful program demands attention to the above factors. ^{sp} The teaching function has as its objectives both medical students and professional workers, through the following media: informal genetics instruction in the offerings of the anatomy department (gross anatomy, embryology, microscopic anatomy); an elective course and graduate program in medical genetics; consultation and clinical demonstration. Emphasis will be placed on those aspects of medical genetics most important in diagnosis, prognosis, and clinical and physiological investigation, so as to stimulate an awareness of significant genetic problems and methods in medical practice and research.

The experimental program is conditioned by my previous background, which has been largely in statistical aspects. As a broad approach to physiological genetics, I have arranged with Professor Lederberg to collaborate during the next year on the genetics of lactase production in *Escherichia coli*. Previous work in his laboratory has established that there are as many as seven distinct and easily separable loci controlling lactase in *E. coli*. The mutants are not identical in their physiological changes, although they all involve lactase, and each locus represents a cluster of closely linked pseudocalleles, some of

which show position effects in diploids. This system could not be adequately worked out for technical reasons, but during the last five years new methods have been developed for a more detailed analysis from both a genetic and physiological standpoint, through greatly increased recombination frequencies and more inclusive transduction. The problems now accessible to investigation include genetic mapping and patterns of position effect in relation to specific physiological differences, including level of residual enzyme, inducibility by various substrates, rate of residual enzyme synthesis, "crypticity" of enzyme in intact vs. disrupted cells, differential temperature effects, changes in enzymatic specificity, and involvement of other enzymes.

Depending on the outcome of this experience and the development of other activities in the medical school during the coming year, this program may be developed in either of two ways: as the initiation of a full scale experimental program in microbial genetics, or as a background to physiological studies in man. The progress of microbial genetics has depended to a considerable extent on selection of easily distinguishable metabolic defects, and the possibility exists that a more systematic search for genetic blocks in known enzymatic steps would be fruitful in human genetics.

In a practical sense, the most important function of this appointment is to stimulate an awareness of the existence of important genetic problems and techniques in clinical investigations, and to try to instigate close collaboration with other workers in various departments of the medical school. For the success of this effort it is essential that there be an effective liaison with the interested departments. This aspect of the geneticist's program needs the most search time for development, and the extent to which it will direct his research activities is difficult to foresee.

I have been working for the past two years on human linkage and recently on statistical problems in the analysis of cattle blood groups, which are closely similar to some hitherto neglected problems in man. These studies can be extended, but the phases with which I have been concerned will terminate before this appointment begins. I plan to suspend work in this direction pending the development of the project in physiological genetics and assessment of the immediate prospects of collaboration in existing clinical investigations.